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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,416	04/13/2000	MICHEL REVEL	REVEL=15	5069

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EXAMINER

KOLKER, DANIEL E

ART UNIT PAPER NUMBER

1649

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/462,416

Applicant(s)

REVEL ET AL.

Examiner

Daniel Kolker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4, 6 - 7, 9 - 11, 16 - 26, 33, and 37 - 38 is/are pending in the application.
- 4a) Of the above claim(s) 16 - 26 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4, 6-7, 9 - 11, 33, 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 4,6,7,9-11,16-26,33,37 and 38 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 January 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/1/05</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's remarks and amendments filed 1 August 2005 have been entered. Claims 1 – 3, 5, 8, 12 – 15, 27 – 32, 34 – 36, and 39 – 44 are cancelled. Claims 4, 6 – 7, 9 – 11, 16 – 26, 33, and 37 – 38 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

3. Claims 16 – 26 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 29 October 2001.

On p. 10 of the remarks filed 1 August 2005 applicant argues that the generic claims are allowable and thus all other claims should be rejoined. However there is no allowable generic or linking claim as explained herein. Thus claims 16 – 26 and 37 remain withdrawn.

Information Disclosure Statement

4. On p. 11 of the remarks filed 1 August 2005, applicant indicates that MPEP 609III A(3) states that the submission of an English language abstract may fulfill the requirement for a concise explanation. Applicant has submitted the abstract of WO9732891 as well as a translation of the claims, which appears in EO0888384. The abstract and claims have been considered. However the WO9732891 publication is not in English and thus has not been considered in its entirety. While the paragraph of MPEP cited by applicant does indicate that an abstract may fulfill the requirement for a concise explanation, the paragraph which appears directly above it states "If no translation is submitted, the examiner will consider the information in view of the concise explanation and insofar as it is understood on its face, e.g., drawings, chemical formulas, English language abstracts, in the same manner that non-English language information in Office search files is considered by examiners in conducting searches." In this case, the English language abstract and claims and other information from WO9732891 which is readily understood by the examiner has been considered, but the entirety of the application cannot be considered as it is not in English and applicant has not provided a translation.

Withdrawn Rejections and Objections

5. The following rejections and objections made in the previous office action are withdrawn:

The rejections of claims 4, 9 – 11, 33, and 38 under 35 USC 112, first paragraph for not being enabled over the full scope of the claims.

The rejections of claims 4, 9 – 11, 33, and 38 under 35 USC 112, first paragraph for failing to meet the written description requirement.

The rejection of claims 9 – 11, 33, and 38 under 35 USC 103. However see the rejection necessitated by amendment, below.

Rejections and Objections Necessitated by Amendment

Claim Rejections - 35 USC § 112

6. Claims 4, 6 – 7, 9 – 11, 33, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 38, from which all other claims depend, has been amended and is now drawn to a narrower genus than the previous claim. The examiner is not able to find support for the limitation “which linker does not prevent the chimeric polypeptide from triggering dimerization” in conjunction with the scope of the instantly-claimed polypeptides. While linkers of 3 – 4 amino acids are contemplated on p. 7 lines 19 – 21, this is in conjunction with sIL-6R/IL-6 proteins, not the delta-Val construct claimed herein.

7. Claims 4, 6 – 7, 9 – 11, 33, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38, from which all other claims depend, is indefinite because it recites sIL-6R-deltaVal-IL-6. This term appears throughout the specification, but is never defined in a limiting fashion. A skilled artisan would not be able to determine the metes and bounds of claim 38 or any of the claims that depend from it in the absence of a clear definition. Furthermore, the use of the Greek letter delta is confusing. In the art, the use of a delta in a protein name generally indicates that certain residues have been deleted. For example, Chen et al. (1997. Proc Natl Acad Sci USA 94:6910 – 6915) use the delta character to indicate that certain domains have

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been deleted from proteins involved in interleukin signaling (see particularly Figure 4, p. 6913). In the specification, the delta character is used when an amino acid sequence is added (see for example p. 8 lines 3 – 6, wherein three amino acids are added after Val356 of sIL-6R). Thus recitation of the term “sIL-6RdeltaVal” is confusing.

Claim 38 is also deemed to be indefinite because the preamble of the claim is drawn to a chimeric sIL-6R/IL-6 polypeptide, but the body of the claim recites sIL-6R-deltaVal fused to IL-6. Since the term “deltaVal” is not explicitly defined in the specification, it is not clear whether the genus of sIL-6R is coextensive with sIL-6R-deltaVal, or whether the former is a broader genus than the latter.

Claim Rejections - 35 USC § 103

8. Claims 6, 9 – 11, 33, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (1995. Nature Biotechnology 15:142 – 145), in view of Weich et al. (1993. Experimental Hematology 21:647-655).

Claim 38 is drawn to a chimeric sIL-6R/IL-6 fusion protein, transcribed from a single nucleic acid sequence, which includes the Ig domain and receptor pre-membrane domains of sIL-6R and which includes residues 323 – 356 of sIL-6R, and which, in one embodiment, has a 3 – 4 amino acid linker. Claim 6 is also drawn to this linker. Claims 9 – 11 are product-by-process claims, and claim 33 is drawn to a composition comprising the protein of claim 38. While claim 38 recites the limitation “sIL-6R-deltaVal” it is not immediately apparent what this part of the molecule is, or how it differs from the soluble forms of the IL-6 receptor which were known in the art.

Fischer et al. teach a chimeric fusion protein comprised of a shortened version of sIL-6R, a peptide linker, and IL-6. The examiner acknowledges that Fischer et al. do not teach the complete sIL-6R, although they do contemplate its use. See specifically p. 142, third paragraph, which states “[w]e demonstrate that covalently linking human IL-6 to the human sIL-6R results in a highly biologically active fusion protein”, and the fourth paragraph, which describes the construction of the fusion protein. The fusion peptide made by Fischer et al. includes a truncated form of sIL-6R. However, Fischer et al. do not indicate that this truncation confers any advantage, or even difference, over other known forms of sIL-6R. In fact, Fischer et al. teach that the N-terminal region of sIL-6R, including the Ig domain, and the C-terminal tether domain (i.e. receptor pre-membrane domain) do not contribute to the protein's biological activity (p. 143,

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end of paragraph that begins on p. 142). Furthermore, circular dichroism spectroscopy shows that the fusion protein folds as one would predict a product composed of isolated IL-6 and IL-6R would (p. 143, first complete paragraph). Fischer et al. do not teach 3 – 4 amino acid peptide linkers.

Weich et al. teach fusion proteins between IL-3 and erythropoietin (Epo), using linkers either 2 – 3 or 23 amino acids long. Weich teaches that the size and flexibility of the linker does not alter the function of the chimeric protein (see p. 651 second column). It would have been prima facie obvious to one of ordinary skill in the art to make a fusion protein between the sIL-6R and IL-6, as taught by Fischer, as long as the sIL-6R part of the molecule includes residues 113 – 323. Including additional residues beyond these do not matter, even if they are part of a naturally occurring isoform, as Fischer teaches that the omitted sequences do not confer additional activity.

It would also have been obvious to one of ordinary skill in the art to use a 3 – 4 amino acid linker, with a reasonable expectation of success. Weich teaches 3-amino acid linkers in the construction of chimeric interleukin molecules, and teaches that the linker used does not affect the function of the molecule. Thus selection of any linker, including those disclosed by Weich, are within the skill of the ordinary artisan. See MPEP § 2144.05, "Overlap of Ranges" and § 2144.06, "Substituting Equivalents Known for the Same Purpose".

Claim 33 is drawn to a pharmaceutical composition with the polypeptide of claim 38 as an active ingredient, and a pharmaceutically acceptable carrier. Claim 38 has been rejected under 35 U.S.C. 103. Because Fischer et al. treated cells with a pharmaceutical composition comprising their fusion protein (see Figures 4 – 6, for example), the teachings of Fischer meet the limitation of claim 33 as well.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.

September 28, 2005


SHARON TURNER, PH.D.
PRIMARY EXAMINER
10-5-05